

## CLAIMS

I/We claim:

- [c1]            1.     A method for determining an alternan signature estimate obtained from a physiological signal having substantially repeating physiologic waveforms representative of a subject's heart activity, the method comprising:
- (a)   identifying T-wave segments of the repeating physiological waveforms;
  - (b)   computing estimated alternan signatures between temporally adjacent T-wave segments by differencing the temporally adjacent T-wave segments while maintaining consistent alternan polarity of the difference;
  - (c)   smoothing the estimated alternan signatures to obtain smoothed alternan estimates; and
  - (d)   identifying a data set from the smoothed alternan estimates that represents a final alternan signature estimate curve.
- [c2]            2.     The method of claim 1 further comprising repeating procedures (a) through (d) for each of a plurality of signals representative of a subject's heart activity.
- [c3]            3.     The method of claim 1 further comprising acquiring the physiological signal while performing a stress test on the subject.
- [c4]            4.     The method of claim 1 further comprising acquiring the physiological signal by obtaining ECG data of the subject's heart.

- [c5]           5.     The method of claim 1 wherein identifying the T-wave segments comprises (a) determining an average/median beat estimate having a QRS complex and a T-wave segment and (b) cross-correlating the QRS complexes of the repetitive waveforms with the QRS complex of the average/median beat estimate to align the beats.
- [c6]           6.     The method of claim 1 wherein identifying T-wave segments comprises temporally identifying an onset and a conclusion of individual T-wave segments.
- [c7]           7.     The method of claim 1 wherein identifying T-wave segments comprises temporally identifying an onset and a pre-determined T-wave duration to set a time-defined conclusion of at least some of the T-wave segments.
- [c8]           8.     The method of claim 1 further comprising aligning a plurality of the T-wave segments before computing the estimated alternan signatures.
- [c9]           9.     The method of claim 8 wherein aligning the T-wave segments comprises using a consistently identifiable portion common to several of the repeating waveforms to temporally align the T-wave segments before computing the estimated alternan signatures in procedure (b).
- [c10]          10.    The method of claim 1 further comprising determining a beat estimate from the repeating physiological waveforms and using the beat estimate to establish a best estimate for the onset of the T-wave segments.
- [c11]          11.    The method of claim 10 wherein the best estimate for the onset of the T-wave segments comprises a time-window definition for identifying the T-wave segments.

- [c12] 12. The method of claim 1 wherein the physiologic signal is processed to reduce noise and/or computational overhead during smoothing of the plurality of estimated alternan signatures.
- [c13] 13. The method of claim 1 wherein smoothing the estimated alternan signatures in procedure (c) comprises reducing the data representative of the estimated alternan signatures by establishing a plurality of data subsets and determining for individual data subsets an average value, a median value and/or a value based upon the midpoint of a curve fitted through the data of a data subset.
- [c14] 14. The method of claim 1 wherein smoothing the estimated alternan signature in procedure (c) comprises reducing the number of data points by a factor of between about 5 to 30.
- [c15] 15. The method of claim 1 wherein at least one data set is identified from the estimated alternan signatures.
- [c16] 16. The method of claim 1 wherein identifying a data set in procedure (d) comprises computing at least one of an average estimate of the plurality of estimated alternan signatures or a median estimate of the plurality of estimated alternan signatures to derive at least one smoothed alternan estimate.
- [c17] 17. The method of 16 wherein one of the average estimate or the median estimate is compared with individual smoothed alternan estimates to determine a weighting factor, and further comprising applying the weighting factor to individual smoothed alternan estimates to determine a weighted average alternan estimate representing the final alternan signature estimate curve.

- [c18] 18. The method of 17 wherein the weighting factor includes a computation of the root mean square difference between one of the average estimates or the median estimate and individual smoothed alternan estimates.
- [c19] 19. The method of claim 1 further comprising identifying and correcting reversals in the polarity of an alternan component of the physiologic signal.
- [c20] 20. The method of claim 1 wherein data sets are constructed from the plurality of smoothed alternan estimates to represent the alternan signature temporally before and after possible disruptions in a polarity of an alternan component of the physiologic signal.
- [c21] 21. The method of claim 20 wherein a polarity reversal is detected if the similarity between data sets before and after the possible disruption is less than the similarity between the data sets when one of the data sets is multiplied by (-1).
- [c22] 22. The method of claim 21 wherein the method of computing similarity between the data sets is preformed through a cross-correlation method.
- [c23] 23. The method of claim 20 where the data set following a disruption is corrected for a polarity reversal by multiplying the associated plurality of smoothed alternan estimates by (-1).
- [c24] 24. The method of claim 23 whereby the possible disruption is associated with premature heartbeats, pauses and/or disruptions to baseline cardiac activity of the subject's beat.

[c25] 25. A method of determining alternations of T-waves using a signal having repeating waveforms corresponding to heart activity of a person, the method comprising:

generating T-wave signal data by sampling the signal at a rate greater than approximately 2000 samples per second and selecting T-wave segments from the T-wave signal data;

computing individual estimated alternan waveforms for temporally adjacent T-wave segments;

ascertaining a reference alternan waveform from the individual estimated alternan waveforms; and

determining a final alternan waveform based on the individual alternan waveforms and the reference waveform.

[c26] 26. The method of claim 25 wherein computing individual estimated alternan waveforms further comprises smoothing the individual estimated alternan waveforms.

[c27] 27. The method of claim 26 wherein smoothing the individual estimated alternan waveforms comprises establishing data subsets for the individual estimated alternan waveforms and determining a representative value for each subset.

[c28] 28. The method of claim 27 wherein determining a representative value for each subset comprises computing an average value, a median value and/or a value based on the midpoint of a curve fitted through each subset.

[c29] 29. The method of claim 25 wherein ascertaining a reference alternan waveform comprises determining an average waveform and/or median waveform of the individual estimated alternan waveforms.

[c30] 30. The method of claim 25 wherein determining a final alternan waveform comprises computing a weighted average waveform and/or a weighted median waveform.

[c31] 31. The method of claim 25 wherein:  
ascertaining a reference alternan waveform comprises determining an average waveform and/or median waveform of the individual estimated alternan waveforms; and  
determining a final alternan waveform comprises computing a weighted average waveform and/or a weighted median waveform by (a) differencing the individual estimated alternan waveforms with the reference waveform, (b) weighting individual estimated waveforms such that individual estimated waveforms with larger differences from the reference waveform are weighted less than those with smaller differences from the waveform, and (c) computing a weighted average alternan waveform defining the final alternan waveform.

[c32] 32. The method of claim 31 wherein differencing the individual estimated alternan waveforms with the reference waveform comprises determining the root mean square differences between the individual estimated alternan waveforms and the average waveform and/or the median waveform.

[c33] 33. A method of detecting the presence of alternations in T-waves using a signal corresponding to heart activity of a person, the method comprising:  
calculating differences at relative time intervals of selected T-wave segments of the signal to provide preliminary alternan waveforms;  
compensating for disturbances and/or ectopic beats in the preliminary alternan waveforms; and

computing a final alternan waveform.

[c34] 34. The method of claim 33 wherein compensating for disturbances comprises smoothing the preliminary alternan waveforms.

[c35] 35. The method of claim 34 wherein smoothing the preliminary alternan waveforms comprises establishing data subsets for individual preliminary alternan waveforms and determining a representative value for each subset.

[c36] 36. The method of claim 35 wherein determining a representative value for each subset comprises computing an average value, a median value and/or a value based on the midpoint of a curve fitted through each subset.

[c37] 37. The method of claim 33 wherein computing a final alternan waveform comprises computing a weighted average waveform and/or a weighted median waveform.

[c38] 38. The method of claim 33 wherein computing a final alternan waveform comprises:

ascertaining a reference alternan waveform by determining an average waveform and/or median waveform of the preliminary alternan waveforms; and

determining a final alternan waveform comprises computing a weighted average waveform and/or a weighted median waveform by (a) differencing individual preliminary alternan waveforms with the reference waveform, (b) weighting each preliminary alternan waveform such that preliminary alternan waveforms with larger differences from the reference waveform are weighted less than those with smaller differences from the reference waveform, and (c)

computing a weighted average alternan waveform defining the final alternan waveform.

[c39] 39. The method of claim 38 wherein differencing individual preliminary alternan waveforms with the reference waveform comprises determining the root mean square differences between each preliminary alternan waveform and the average waveform and/or the median waveform.

[c40] 40. A system for determining alternations of T-waves using a signal having repeating waveforms corresponding to heart activity of a person, comprising:

- a data source configured to obtain electrophysiological data having repeating waveforms corresponding to heart activity of a person; and

- a computer operatively coupled to the data source, the computer having a computer operable medium containing instructions that (a) selects T-wave segments from the electrophysiological data, (b) computes individual estimated alternan waveforms for temporally adjacent T-wave segments, (c) ascertains a reference alternan waveform from the individual estimated alternan waveforms, and (d) determines a final alternan waveform based on the individual alternan waveforms and the reference waveform.

[c41] 41. The system of claim 40 wherein the instructions further comprise computing individual estimated alternan waveforms by smoothing the individual estimated alternan waveforms.

[c42] 42. The system of claim 40 wherein smoothing the individual estimated alternan waveforms comprises establishing data subsets for the individual



estimated alternan waveforms and determining a representative value for each subset.

[c43] 43. The system of claim 42 wherein determining a representative value for each subset comprises computing an average value, a median value and/or a value based on the midpoint of a curve fitted through each subset.

[c44] 44. The system of claim 40 wherein the instructions for ascertaining a reference alternan waveform further comprise determining an average waveform and/or median waveform of the individual estimated alternan waveforms.

[c45] 45. The system of claim 44 wherein the instructions for determining a final alternan waveform comprises computing a weighted average waveform and/or a weighted median waveform.

[c46] 46. The system of claim 40 wherein:  
the instructions for ascertaining a reference alternan waveform comprise  
determining an average waveform and/or median waveform of the  
individual estimated alternan waveforms; and  
the instructions for determining a final alternan waveform comprises  
computing a weighted average waveform and/or a weighted median  
waveform by (a) differencing the individual estimated alternan  
waveforms with the reference waveform, (b) weighting individual  
estimated waveforms such that individual estimated waveforms with  
larger differences from the reference waveform are weighted less  
than those with smaller differences from the reference waveform, and  
(c) computing a weighted average alternan waveform defining the  
final alternan waveform.

[c47]            47.    The system of claim 46 wherein differencing the individual estimated alternan waveforms with the reference waveform comprises determining the root mean square differences between the individual estimated alternan waveforms and the average waveform and/or the median waveform.